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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/665,373	09/22/2003	Hidehiro Yamazaki	033025-006	5015

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EXAMINER	
PAK, JOHN D	
ART UNIT	**PAPER NUMBER**
1616	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	01/18/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/665,373	YAMAZAKI, HIDEHIRO	
	Examiner	Art Unit	
	JOHN PAK	1616	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 October 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-8 and 10-16* is/are pending in the application.

4a) Of the above claim(s) *5-8,10-14 and 16* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4 and 15* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on 9/22/03 is/are: a)☐ accepted or b)☒ objected to by the Examiner. –See PTO-948

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Claims 1-8 and 10-16 are pending in this application. Claim 16 is new.

New claim 16 is directed to a pharmaceutical composition. This invention was restricted as the non-elected invention of Group VIII in the Office action of 1/26/2006 and in applicant's election of Group VI in the response of 2/27/2006. Accordingly, claim 16, as well as claims 5-8 and 10-14, are hereby withdrawn as being directed to non-elected subject matter. Claims 1-4 and 15 will presently be examined to the extent that they read on the elected subject matter.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 4 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 4 has been amended to recite, "wherein said patient supervenes metabolic acidosis." This is an incorrect and confusing use of the verb "supervenes." The patient cannot follow or supervene metabolic acidosis. Some other condition in a patient could follow or supervene acidosis but not the patient herself.

Applicant is advised that the outstanding ground of rejection under 35 USC 102(b) over JP 10-203961 is hereby withdrawn because, upon reconsideration and in view of applicant's amendments and arguments, the reference does not explicitly disclose the claimed rate of 2-60 ml/kg/hour administered to a patient undergoing an operation or a postoperative patient.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-4 and 15 are rejected under 35 U.S.C. 103(a) as being unpatentable over JP 10-203961 in view of Medline abstract 93060291, HCAPLUS abstract 1984:188290 and HCAPLUS abstract 1997:400035.

JP 10-203961[1] discloses treating ketoacidosis, without causing alkalosis, by administering a solution that contains the following electrolytes:

sodium: 120-150 mEq/L;

potassium: 0-10 mEq/L;

chloride : 90-120 mEq/L ;

calcium : 0-5 mEq/L;

magnesium: 0-5 mEq/L;

bicarbonate: 20-35 mEq/L;

citrate: 1-5 mEq/L.

See machine Translation of claim 1 and paragraphs 5, 8-9; see also HCAPLUS Abstract 1998:498580. Correction of acidosis with bicarbonate is generally disclosed (machine translation of paragraphs 2-3). The electrolyte solution set forth above is administered

[1] This is a Japanese language document. For applicant's convenience, a full machine translation and also an English language abstract, HCAPLUS Abstract 1998:498580, is provided

as an infusion[2] at the time of "surgical stress" to provide electrolyte balance (machine translation of paragraph 13). Dose is taught to be suitably adjusted according to a patient's symptoms, age, weight, etc., at 500-8000 ml/per day (id.). Administration rate of 60 ml/kg/hr and higher rates are exemplified (machine translation of paragraph 17).

Medline abstract 93060291 discloses that hormonal change after surgical stress and anaerobic glucolysis due to tissue ischemia cause acidosis. Postoperative complications also cause acidosis. Acidosis is specifically found in gastrointestinal surgery. Alkalosis is discussed as a result of bicarbonate production from lactate and citrate supplied by massive infusion and transfusion.

HCAPLUS abstract 1984:188290 discloses that the use of blood gas analytical parameters for monitoring and therapy of patients with acid-base disturbances is known.

HCAPLUS abstract 1997:400035 discloses an apparatus capable of determining CO_2 partial gas pressure and pH from blood gas analysis for clinical diagnosis. The apparatus is "convenient for monitoring acidosis or alkalosis."

Controlling electrolyte balance is explicitly taught by JP 10-203961, and controlling water balance would be obtained from the administration of the same exact solution. The patient in JP 10-203961 suffers from ketoacidosis, which is a type of metabolic acidosis, **and can include patients under surgical stress**. The makeup of the solution in JP 10-203961 compares as follows with applicant's invention:

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[2] "[T]ransfusion" in the machine translation, e.g., paragraph 13, which would have been understood by a skilled artisan in this field as an infusion.

	JP 10-203961	Applicant's claimed invention
sodium:	120-150 mEq/L	130-145 mEq/L
potassium:	0-10 mEq/L	2-5 mEq/L
chloride :	90-120 mEq/L	90-130 mEq/L
calcium :	0-5 mEq/L	2-5 mEq/L
magnesium:	0-5 mEq/L	0.5-2.5 mEq/L
bicarbonate:	20-35 mEq/L	20-35 mEq/L
citrate:	1-5 mEq/L	1-7 mEq/L.

It is the Examiner's position that the concentration of the claimed invention would have been fairly suggested to the ordinary skilled artisan in this field from the narrow range of identical components disclosed by JP 10-203961. Even if it could be argued that the solution in JP 10-203961 does not match exactly in content, one having ordinary skill in the art would have been motivated to adjust from the narrow range taught by JP 10-203961 the solution makeup and concentration as claimed to control water and electrolyte balance and acid-base equilibrium in patients suffering from metabolic acidosis and surgical or postoperative patient. The motivation for such adjustment would come from monitoring and responding to the patient's blood parameters, which must be done when treating acid imbalance.

As for the claimed feature of 2-60 ml/kg/hour, the Examiner's position is that such infusion speed is fairly suggested. 60 ml/kg/hr is exemplified by JP 10-203961 (paragraph 17). Additionally, the reference discloses 500-8000 ml/per day, which is to be adjusted according to a patient's symptoms, age, weight, etc. To the ordinary skilled artisan, the claimed 2-60 ml/kg/hour feature would have been obvious from the reference disclosure since determining how much of the infusion to administer or how fast to administer would depend on patient condition and weight, at least. For example, acute cases of acidosis would indicate higher infusion speed because more bicarbonate

would be needed to more quickly counteract the greater degree of acidosis. And as the patient stabilizes, the ordinary skilled artisan would have been motivated to adjust the infusion speed lower or demedicate because the acidosis is already under control. Given such level of the ordinary skill in the art, the following sample calculation would have been obvious:

	8000 ml/day (maximum taught by JP 10-203961)	4000 ml/day (1/2 of maximum taught by JP 10-203961
Typical 80 kg male	4.2 ml/kg/hr	2.1 ml/kg/hr
Typical 60 kg female	5.6 ml/kg/hr	2.8 ml/kg/hr

The calculations above are shown merely to establish that applicant's lower range of infusion speed would have been obvious.

The secondary references HCAPLUS abstract 1984:188290 and HCAPLUS abstract 1997:400035 further establish the motivation of the ordinary skilled artisan to adjust the infusion speed or demedication of the solution as discussed above, because said references establish that close monitoring of the patient's blood parameters via blood gas analysis is practiced when treating acidosis. The secondary reference by Medline abstract further establishes the motivation of ordinary skilled artisan to treat surgical and postoperative patients with the solution taught by JP 10-203961.

As for the feature of claim 3, which requires adjusting infusion speed to maintain a plasma bicarbonate concentration to be in a range of 22 to 26 mEq/L, it is the Examiner's position that such method step is but a truism for virtually all acidosis treatments since the normal plasma bicarbonate concentration in humans is 24 mEq/L.

Therefore, the claimed invention, as a whole, would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made, because every element of the invention and the claimed invention as a whole have been fairly disclosed or suggested by the teachings of the cited references.

Applicant's remarks relative hereto have been given due consideration but they were deemed unpersuasive. Applicant argues that the "unexpectedly superior effects obtained by the method recited in the present invention are not taught or suggested by JP 10-203961." Applicant adds, "the rate of the infusion speed of the preparation can be adjusted or the infusion terminated in order to maintain the blood pH in a range of 7.3 to 7.5 and the plasma bicarbonate concentration in a range of 22 to 26 mEq/L." Several "superior effects" are asserted: acidosis correction effect is exhibited immediately after the start of infusion and metabolic alkadosis and hypernatremia are avoided due to the demedication step.

The Examiner cannot agree. Applicant's specification data shows no such adjustment of infusion speed and/or demedication "based on the blood gas analysis" or plasma bicarbonate concentration of 22-26 mEq/L. There is in fact no adjustment at all. A constant infusion rate or speed is not the same as adjusting the rate or speed. In Example 1, part (a), 60 ml/kg/hour rate is maintained for 90 minutes. No other infusion rate is used. There is absolutely no adjustment, only demedication. Even though Test-20.0 (which reads on the claims) is deemed to provide insufficient acidosis correction, no adjustment, i.e. no increase or decrease in infusion rate, is practiced (specification page 12, lines 1-3). Further, even though the data for Time = 0 shows acidosis, the

infusion rate is the same at Time = 0 and at Time = 60 to almost 90, when acidosis is treated for several of the Test preparations. Similar comments apply to Example 1, part (b), wherein a constant infusion rate of 40 ml/kg/hour for 90 minutes is disclosed. Even though Test-20.0 (which reads on the claims) is again deemed to provide insufficient acidosis correction, no adjustment, i.e. no increase or decrease in infusion rate, is practiced (specification page 13, lines 8-10). Further, even though the data for Time = 0 shows acidosis, the infusion rate is kept constant at Time = 0 and at Time = 60 to almost 90, when acidosis is treated for several of the Test preparations. Similar comments apply to Example 2 since there is no adjustment there, too.

As a result, it can be seen that applicant's specification data establishes nothing related to adjusting infusion speed based on any patient factor, and no "unexpectedly superior effects" can be attributed to such adjustment feature.

Additionally, it is the Examiner's position that comparisons made in the specification are not with respect to the closest prior art. Applicant compared against lactated Ringer's solution and acetated Ringer's solution, but those solutions contain no bicarbonate. The solution taught by JP 10-203961 contains 20-35 mEq/L bicarbonate. Therefore, applicant's data fails to establish nonobvious evidence because the data is not a comparison against the closest prior art.

For these reasons, the claims must be rejected again.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to JOHN PAK whose telephone number is **(571)272-0620.** The Examiner can normally be reached on Monday to Friday from 8 AM to 4:30 PM.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's SPE, Johann Richter, can be reached on **(571)272-0646**.

The fax phone number for the organization where this application or proceeding is assigned is **(571)273-8300**.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571)272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only.

For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

John Pak
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